UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/646,361 | 08/21/2003 | Xian-Ming Zeng | TEVE-121US | 8629 |

23122 7590 05/12/2011

RATNERPRESTIA
P.O. BOX 980
VALLEY FORGE, PA 19482

| EXAMINER | |
|---|---|
| ALSTRUM ACEVEDO, JAMES HENRY | |
| ART UNIT | PAPER NUMBER |
| 1616 | |
| MAIL DATE | DELIVERY MODE |
| 05/12/2011 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/646,361 | ZENG, XIAN-MING | |
| | Examiner | Art Unit | |
| | JAMES H. ALSTRUM ACEVEDO | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

**Claims 1-15 are pending**. Applicant amended claim 15. Claim 15 is withdrawn from consideration. **Claims 1-14 are under consideration** in the instant office action. Applicant is advised that a different Examiner is examining the instant application. Receipt and consideration of Applicant's amended claim set and arguments/remarks submitted on April 4, 2011 are acknowledged. All rejections/objections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments and/or persuasive arguments.

### *Election/Restrictions*

Newly submitted amended claim 15 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claimed composition of claim 1 can be prepared by a materially different method, such as by spray drying components (a) and (b) separately and mixing the resulting powders to obtained the claimed composition.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, **claim 15 is withdrawn from consideration** as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in the United Kingdom on August 21, 2001. It is noted, however, that applicant has not

filed certified copies of GB 0219513.7 and GB 0219513.9 application as required by 35 U.S.C. 119(b).

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. (US 6,645,466) in view of Ward et al. (US 6,616,914).**

### *Applicant Claims*

Applicant claims a dry powder inhalation composition comprising, (a) medicament particles, and (b) a mixture of lactose particles with a VMD of between about 70 and about 120 microns and a diameter of less than 250 microns, wherein up to 96% by weight of the lactose

particles are less than 150 microns in diameter and wherein up to 25% by weight of the lactose particles are less than 5 microns in diameter.

***Determination of the scope and content of the prior art (MPEP §2141.01)***

Keller et al. teach **dry powder formulations for inhalation and delivery to the lung** comprising a pharmaceutically ineffective carrier of not-inhalable size and a finely divided pharmaceutically active compound of inhalable particle size (see the abstract, column 1, lines 16-21, and the Examines). **The pharmaceutically active compound of an inhalable size has a mean mass aerodynamic diameter (MMAD) of at most 10 microns** (see column 4, lines 56-67 and column 6, lines 2-7). The particles can be prepared by spray- drying or micronization (see column 6, lines 7- 12). Examples of pharmaceutical actives include formoterol, fenoterol, etc. (see column 6, lines 13-37). One or more actives may be used see column 6 lines 35-37). **The actives are present in an amount of 0.1 to 10% by weight of the formulation** (see column 7 lines 11-21). **The non-inhalable coarse carrier particles have a mean mass aerodynamic diameter (MMAD) of about 10 to 500 microns** (see column 7, lines 40-53). **The formulation can also contain a proportion of inhalable carrier particles having a particle size diameter (as (MMAD) of at most 10 microns and are present in the formulation in an amount of 0.1 to about 10% by weight** (see column 8, lines 8-16, and claims 1-6). **The carrier material may be present in a total amount of 80 to 99.9% by weight** (see column, 8 lines 22-25). **Examples of the carrier include lactose** (see column 5, lines 58-65 and column 8, lines 1-9). The optimum particle size of the carrier depends on the demands and specifications of the powder inhaler intended for administration of the formulation

(see column 7, lines 40-53). **Examples 1-6 teach lactose monohydrate having a broad range of particle size distribution**.

Ward teaches **a method for oral and pulmonary delivery of pharmaceuticals, wherein a powder formulation for use in a dry powder inhaler (DPI) comprises a pharmaceutical, which acts as its own carrier and is present as (a) microfine particles having an average volume median diameter in the range of 1-10 microns and larger carrier particles that have an average volume median diameter of 10-2,000 microns, preferably 30-300 microns, and most preferably from 50-100 microns in diameter**. Ward also teaches that the administration of the composition results in both a rapid onset pharmaceutical effect and a slower onset pharmaceutical effect (see abstract, column 2, lines 20-25 and 51-56, and claims 1-23). Ward teaches that **suitable medicaments for use in the invented formulations include beta-agonists (i.e. a known class of bronchodilators), such as albuterol, anti- inflammatories, and drugs for treating COPD and other diseases** (see column 4, lines 21-28). Ward teaches that the invented **composition is desirable to improve patient compliance for patients taking more than one pharmaceutical** (see column 1, line 60 through column 2, line 13) and that, in general, inert carrier particles such as lactose upon inhalation administration are caught in the mouth and throat, swallowed, and exert no pharmaceutical effect (column 3, lines 5-12).

***Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)***

Keller lacks the teaching of carrier particles having a volume median diameter ranging between 70-120 microns. This deficiency is cured by Ward.

***Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)***

A person of ordinary skill in the art would have been motivated to make a dry powder formulation comprising lactose particles having a volume median diameter ranging between 70 and 120 microns because it is known in the art that dry powder inhalation formulations comprising lactose carrier particles having a volume median diameter ranging from preferably about 30 to 300 microns can deliver active compounds to the lungs with a fasting acting or rapid onset of effect, as suggested by Ward et al. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a dry powder formulation with lactose particles having a volume median diameter (VMD) ranging between 70 and 120 microns because it is an obvious VMD range that can be used in the preparation of dry powder formulations for delivery of an active to the lungs. It is noted that Ward et al. do not teach up to 96% by weight of lactose particles having a particles size less than 150 microns or up to 25% by weight of lactose particles having a particles size less than 5 microns. However, Keller et al. do suggest that 10% of the carrier particles can have a particle size of at most 10 microns (see column 8 lines 9-16). Keller et al. also teach formulations comprising lactose of various particle sizes and suggest that the optimum particle size of the carrier depends on the demands and specifications of the powder inhaler intended for administration of the formulation (see column 7, lines 40-53 and the Examples). Absent a clear showing of criticality of the percentages as claimed, the determination of particular concentrations is within the boundaries of routine experimentation of one skilled in the art as part of the process of normal optimization to achieve the desired dry powder formulation.

With respect to claim 15, "wherein said portion of coarse lactose particles is prepared by a method comprising collecting lactose particles on a mesh with mesh size of 63 microns after passing through a mesh with mesh size of 90 microns" it is noted that Keller et al. do not specifically teach the instantly claimed method of preparation. However, the patentability of a product does not depend on its method of production. If the product in the product- by-process claims is the same or obvious from a product in the prior art, the claim will be held unpatentable even if the prior product is made by a different process (See MPEP 2113). Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

***Response to Arguments***

Applicant's arguments filed April 4, 2011 have been fully considered but they are not persuasive. Applicants traverse the instant rejection by arguing that the rejection is flawed because allegedly (i) no reason for the combination of references was provided in the office action; (ii) the Ward reference teaches away because it focuses on the use of a pharmaceutical agent as its own carrier; and (iii) the combined prior art references do not refer to volume mean diameter, but rather volume median diameter, which Applicants assert are different characterizations of the particle size distribution.

The Examiner respectfully finds Applicant's arguments unpersuasive. Regarding (i) and (iii), the combination of references is premised on the notion that Ward establishes suitable volume median diameter ranges for carriers used in inhalable formulations. It is noted that

although Keller is silent as to the volume median diameter and volume mean diameter this does not mean that Keller's powders do not exhibit a volume median diameter or volume mean diameter. The Examiner concedes that volume median diameter is not necessarily equivalent to a volume mean diameter, but nonetheless, because the numerical ranges of volume median diameter taught by Ward overlap with the numerical volume mean diameter ranges recited by Applicant it is reasonable to conclude that the volume mean diameter ranges resulting from the combined prior art references would also substantially overlap with those recited in Applicant's claims. Applicant has provided no objective evidence that compositions made according to the teachings of the combined prior art comprising lactose carrier and having the volume median diameter ranges taught by Ward as being suitable for a carrier would not have volume mean diameter ranges that are overlapping with the volume mean diameter ranges recited in Applicant's claims.

Regarding (ii), Ward does not teach away from the general use of lactose as an inert carrier in inhalable formulations. Applicant is correct that in Ward's compositions the active functioned both as a carrier and an inhalable active based on the two different particle sizes of the active agent. Nonetheless, this does not teach away from the suitability of a carrier having the volume median diameter ranges taught by Ward or the use of an inert carrier in general, because Ward does not discourage or discredit the use of an inert carrier, such as lactose, in inhalable formulations. Ward was relied upon to demonstrate volume median diameter ranges that an ordinary skilled artisan would recognized are suitable for carrier used in inhalable formulations. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

### *Conclusion*

**Claims 1-14 are rejected. Claim 15 is withdrawn by original presentation. No claims are allowed.**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, ~10:00-6:00 and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JAMES H. ALSTRUM-ACEVEDO/ J.H. Alstrum-Acevedo, Ph.D.
Primary Examiner, Art Unit 1616
Technology Center 1600